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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,331	10/08/2003	David L. Shelton	514712000400	8299

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/682,331	SHELTON ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *7 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/9/04,12/8/05,9/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-6, drawn to a method for treating post-surgical pain comprising administering an antagonist of nerve growth factor (NGF) wherein the NGF antagonist is other than TrkA immunoadhesin, in the reply filed on 28 June 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 8-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 28 June 2006. The Examiner recognizes Applicant's right to pursue additional subject matter in other applications. Therefore, claims 1-8 are pending, and claims 1-6, as they read upon the elected species kinase inhibitor, are under consideration and the subject of this Office Action.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on 09 July 2004, 18 December 2005, and 06 September 2006 have been considered by the Examiner. The following references have been considered to the extent of the abstract only, as the remainder of the references are not in the English language: references 83 and 89 from the IDS filed 09 July 2004, and references 27-31 from the IDS filed 06 September 2006.

Specification

4. The disclosure is objected to because of the following informalities:

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "METHODS FOR TREATING POST-SURGICAL PAIN BY ADMINISTERING A NERVE GROWTH FACTOR ANTAGONIST".

6. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See for example, page 43 [0112] and pg 44 [0114]. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

35 U.S.C. § 112, Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claim does not have a step that clearly relates back to the preamble. For example, there is no step indicating the treatment of post-surgical pain.

10. Claims 2 and 3 are rejected as being indefinite for reciting the phrase "suppressed or ameliorated". The terms "suppressed" and "ameliorated" are not defined by the claims, and

since neither the art nor the specification provides an unambiguous definition of the terms, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Specifically, it is unclear if the two terms are intended to encompass the same level/measure of treatment, or if Applicants intend to encompass two different levels/measures of treatment.

11. Claim 2 recites the limitation "wherein resting pain" in line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 2 depends, does not recite "resting pain".

12. Claim 3 recites the limitation "wherein mechanically-induced pain" in line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 1, from which claim 3 depends, does not recite "mechanically-induced pain".

13. With regards to the rejection of claims 2 and 3 (set forth at ¶10 and ¶11 *supra*), it is suggested that an intervening claim which recites "The method of claim 1 wherein surgical pain consists of resting pain or mechanically-induced pain", or the like, would be remedial.

14. Claim 2 is further rejected as being indefinite for reciting the phrase "resting pain". At pg 24 ([0069]) the Specification teaches that "resting pain refers to pain occurring even while the individual is at rest as opposed to, for example, pain occurring when the individual moves or is subjected to other mechanical stimuli". However, at pg 67 ([0171]) the Specification teaches that resting pain was evaluated using a measure of weight bearing. Since the behavioral measure of resting pain in this model involves a mechanical stimulus, i.e., weight bearing, it is unclear what is encompassed by this phrase in the claim.

15. Claim 3 is rejected as being indefinite for reciting the phrase "mechanically-induced pain". At pg 24 ([0070]) the Specification teaches that "mechanically induced pain

(interchangeably termed mechanosensory pain) refers to pain induces [sic] by a mechanical stimulus, such as the application of weight to a surface, tactile stimulus, and stimulation caused or associated with movement". However, at pg 67 ([0171]) the Specification teaches that resting pain was evaluated using a measure of weight bearing. Since the behavioral measure of resting pain in this model involves a mechanical stimulus, i.e., weight bearing, it is unclear what is encompassed by this phrase in the claim.

16. Claim 3 is further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: mechanically inducing pain. Therefore, it is unclear what additional method steps are intended to be encompassed by the claim.

17. Claims 4-6 are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Owolabi et al. (J. Pharmacol. Exp. Ther. 289(3):1271-1276, 1999) in view of Brennan, T.J. (ILAR. 40(3):129-136, 1999; cited by Applicant on IDS filed 9/6/06).

21. Owolabi et al. teach administration of ALE-0540, a nerve growth factor receptor antagonist which inhibits binding of NGF to the NGF receptor TrkA, produces antiallodynia in a rat model of neuropathic pain, and blocks tactile allodynia in an inflammatory pain model in rats.

22. The reference of Owolabi et al. does not teach the administration of ALE-0540 for the treatment of post-surgical pain.

23. Brennan teaches that the mechanisms for initiation and maintenance of pain after incision (i.e., post-surgical pain) likely involve a combination of nerve injury, inflammation, pH changes, and central nervous system plasticity (See pg 133).

24. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the ALE-0540 taught by Owolabi et al. for the treatment of post-surgical pain which would, in the absence of evidence to the contrary, ameliorate both resting pain and mechanically-induced pain.

25. The person of ordinary skill in the art would have been motivated to use the ALE-0540 taught by Owolabi et al. to treat post-surgical pain because surgery is known to cause pain and it is obvious to treat the pain to alleviate discomfort in the patient.

26. The expectation of success is high since blocking NGF activity by inhibiting the binding of NGF with the NGF receptor TrkA with ALE-0540 has been shown to alleviate hyperalgesia in a nerve injury model and an inflammatory pain model as taught by Owolabi et al., and both nerve injury and inflammation are components of incisional (i.e., post-operative) pain as taught by Brennan.

27. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

28. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Owolabi et al. (J. Pharmacol. Exp. Ther. 289(3):1271-1276, 1999) in view of Brennan, T.J. (ILAR. 40(3):129-136, 1999; cited by Applicant on IDS filed 9/6/06) as applied to claims 1-3 above, and further in view of Knüsel et al. (J. Neurochem. 59(6):1987-1996, 1992; cited by Applicant on IDS filed 7/9/04).

29. The teachings of Owolabi et al. and Brennan are summarized above.

30. Neither the Owolabi et al. reference nor the Brennan reference teach the administration of a kinase inhibitor which is capable of inhibiting downstream kinase signaling associated with NGF receptor activity, including K252a, for the treatment of post-surgical pain.

31. Knüsel et al. disclose the kinase inhibitor K252a as well as the inhibition of NGF actions by K252a (See pg 1990, left column; pg 1991, left column).

32. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the kinase inhibitor K252a taught by Knüsel et al. for the

treatment of post-surgical pain which would, in the absence of evidence to the contrary, ameliorate both resting pain and mechanically-induced pain.

33. The person of ordinary skill in the art would have been motivated to use the kinase inhibitor K252a taught by Knüsel et al. to treat post-surgical pain because surgery is known to cause pain and it is obvious to treat the pain to alleviate discomfort in the patient.

34. The expectation of success is high since blocking NGF activity by inhibiting the binding of NGF with the NGF receptor TrkA with ALE-0540, which would inherently inhibit the downstream kinase signaling associated with TrkA receptor activity, has been shown to alleviate hyperalgesia in a nerve injury model and an inflammatory pain model as taught by Owolabi et al., and both nerve injury and inflammation are components of incisional (i.e., post-operative) pain as taught by Brennan.

35. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Double Patenting

36. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re

Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

37. Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of copending Application No. 10/682,638. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 2, and 3 of co-pending application 10/682,638 are drawn to methods for treating post-surgical pain in an individual comprising administering to the individual an effective amount of an anti-nerve growth factor (NGF) antagonist antibody. The claims also recite that resting pain or mechanically-induced pain is suppressed or ameliorated. While claims 1-3 in the instant application are drawn more broadly to the administration of an antagonist of NGF wherein the NGF antagonist is other than TrkA immunoadhesin, it would have been obvious to a person of ordinary skill in the art to use the NGF antagonist antibody of copending Application No. 10/682,638 in the treatment methods disclosed in claims 1-3 of the instant application. The motivation to do so is found in the instant application, which discloses that an anti-nerve growth factor (NGF) antagonist antibody is a preferred embodiment of an NGF antagonist (See pg 10-11[0027]).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Summary

38. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 7:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
September 15, 2006

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud